Exome-wide association study of plasma lipids in >300,000 individuals

Liu, Dajiang J.; Peloso, Gina M.; Yu, Haojie; Butterworth, Adam S.; Wang, Xiao-Yu; Mahajan, Anubha

Published in:
Nature Genetics

DOI:
10.1038/ng.3977

Publication date:
2017

Document Version
Peer reviewed version

Exome-wide association study of plasma lipids in >300,000 individuals

Liu, Dajiang J.; Peloso, Gina M.; Yu, Haojie; Butterworth, Adam S.; Wang, Xiao-Yu; Mahajan, Anubha; Saleheen, Danish; Emdin, Connor; Alam, Dewan S.; Alves, Alexessander Couto; Amouyel, Philippe; Di Angelantonio, Emanuele; Arveiler, Dominique; Assimes, Themistocles L.; Auer, Paul L.; Baber, Usman; Ballantyne, Christie M.; Bang, Lia E.; Benn, Marianne; Bis, Joshua C.; Boehnke, Michael; Boerwinkle, Eric; Bork-Jensen, Jette; Bottinger, Erwin P.; Brandslund, Ivan; Brown, Morris J.; Busonero, Fabio; Caulfield, Mark J.; Chambers, John C.; Chasman, Daniel I.; Chen, Y Eugene; Chen, Yii-Der Ida; Chowdhury, Rajiv; Christensen, Cramer; Chu, Audrey Y.; Connell, John; Cucca, Francesco; Cupples, L. Adrienne; Damrauer, Scott M; Davies, Gail; Deary, Ian J.; Dedoussis, George; Denny, Joshua C.; Dominiczak, Anna F.; Dubé, Marie Pierre ; Ebeling, Tapani; Eiriksdottir, Gudny; Esko, Tõnu; Farmaki, Aliki-Eleni; Feitosa, Mary F.; Ferrario, Marco M.; Ferrieres, Jean; Ford, Ian; Fornage, Myriam; Franks, Paul W.; Frayling, Timothy M.; Frikke-Schmidt, Ruth; Fritsche, Lars G; Frossard, Philippe; Fuster, Valentin; Ganesh, Santhi K.; Gao, Wei; Garcia, Melissa E; Gieger, Christian; Giulianini, Franco; Goodarzi, Mark O.; Grallert, Harald; Grarup, Niels; Groop, Leif C.; Grove, Megan L.; Gudnason, Vilmundur; Hansen, Torben; Harris, Tamara B.; Hayward, Caroline; Hirschhorn, Joel N.; Holmen, Oddgeir L.; Huffman, Jennifer E.; Huo, Yong; Hveem, Kristian; Jabeen, Sehrish; Jackson, Anne U.; Jakobsdottir, Johanna; Jarvelin, Marjo-Riitta; Jensen, Gorm B.; Jørgensen, Marit E.; Jukema, J. Wouter; Justesen, Johanne Marie; Kamstrup, Pia R.; Kanoni, Stavroula; Karpe, Fredrik; Kee, Frank; Khera, Amit V; Klarin, Derek; Koistinen, Heikki A.; Kooner, Jaspal S.; Kooperberg, Charles; Kuulasmaa, Kari; Kuusisto, Johanna; Laakso, Markku; Lakka, Timo A.; Langenberg, Claudia; Langsted, Anne; Launer, Lenore J.; Lauritzen, Torsten; Liewald, David C. M. ; Lin, Li-An; Linneberg, Allan; Loos, Ruth J. F.; Lu, Yingchang; Lu, Xiangfeng; Mägi, Reedik; Malarstig, Anders; Manichaikul, Ani; Manning, Alisa K.; Mäntyselkä, Pekka; Marouli, Eirini; Masca, Nicholas G. D.; Maschio, Andrea; Meigs, James B.; Melander, Olle; Metspalu, Andres; Morris, Andrew; Morrison, Alanna C.; Mulas, Antonella; Müller-Nurasyid, Martina; Munroe, Patricia B.; Neville, Matt J.; Nielsen, Jonas B; Nielsen, Sune F.; Nordestgaard, Børge G.; Ordovas, Jose M.; Mehran, Roxana; O'Donnell, Christoper J; Orho-Melander, Marju; Molony, Cliona M; Muntendam, Pieter; Padmanabhan, Sandosh; Palmer, Colin; Pasko, Dorota; Patel, Aniruddh P.; Pedersen, Oluf; Perola, Markus; Peters, Annette; Pisinger, Charlotta; Pistis, Giorgio; Polasek, Ozren; Poulter, Neil R.; Psaty, Bruce M.; Rader, Daniel J.; Rasheed, Asif; Rauramaa, Rainer; Reilly, Dermot F.; Reiner, Alex P.; Renström, Frida; Rich, Stephen S.; Ridker, Paul M.; Rioux, John D.; Robertson, Neil R.; Roden, Dan M.; Rotter, Jerome I.; Rudan, Igor; Salomaa, Veikko; Samani, Nilesh J.; Sanna, Serena; Sattar, Naveed; Schmidt, Ellen M.; Scott, Robert A.; Sever, Peter; Sevilla, Raquel S; Shaffer, Christian M.; Sim, Xueling; Sivapalaratnam, Suthesh; Small, Kerrin S.; Smith, Albert V.; Smith, Blair; Somayajula, Sangeetha; Southam, Lorraine; Spector, Timothy D.; Speliotes, Elizabeth K.; Starr, John M.; Stirrups, Kathleen E.; Stitziel, Nathan O.; Strauch, Konstantin; Stringham, Heather M.; Surendran, Praveen; Tada, Hayato; Tall, Alan R.; Tang, Hua; Tardif, Jean-Claude; Taylor, Kent D.; Trompet, Stella; Tsao, Philip S; Tuomilehto, Jaakko; Tybjaerg-Hansen, Anne; van Zuydam, Natalie R.; Varbo, Anette; Varga, Tibor V.; Virtamo, Jarmo; Waldenberger, Melanie; Wang, Nan; Wareham, Nick J.; Warren, Helen R.; Weeke, Peter E.; Weinstock, Joshua; Wessel, Jennifer; Wilson, James G.; Wilson, Peter W F; Xu, Ming; Yaghootkar, Hanieh; Young, Robin; Zeggini, Eleftheria; Zhang, He; Zheng, Neil S; Zhang, Weihua; Zhang, Yan; Zhou, Wei; Zhou, Yanhua; Zoledziewska, Magdalena; Howson, Joanna M. M.; Danesh, John; McCarthy, Mark I.; Cowan, Chad A; Abecasis, Goncalo; Deloukas, Panos; Musunuru, Kiran; Willer, Cristen J.; Kathiresan, Sekar; Charge Diabetes Working Group

Title: Exome-wide association study of plasma lipids in >300,000 individuals

Dajiang J Liu, Gina M Peloso, Haojie Yu, Adam S Butterworth, Xiao Wang et al. **Exome-wide association study of plasma lipids in >300,000 individuals. Nature Genetics. Epub 30 October 2017. doi:10.1038/ng.3977**

Authors: Dajiang J. Liu{ HYPERLINK \l "_ENREF_1" \o ", #13" }†, Gina M Peloso{ HYPERLINK \l "_ENREF_2" \o ", #26" }†, Haojie Yu{ HYPERLINK \l "_ENREF_5" \o ", #172" }†, Adam Butterworth{ ADDIN EN.CITE <EndNote><Cite><RecNum>23</RecNum><DisplayText><style face="superscript">6,7</style></DisplayText><record><rec-number>23</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">23</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>145</RecNum><record><rec-number>145</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">145</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The National Institute for Health Research Blood and Transplant Unit (NIHR BTRU) in Donor Health and Genomics at the University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}†, Xiao Wang{ HYPERLINK \l "_ENREF_8" \o ", #173" }†, Anubha Mahajan{ HYPERLINK \l "_ENREF_9" \o ", #152" }†, Danish Saleheen{ ADDIN EN.CITE <EndNote><Cite><RecNum>37</RecNum><DisplayText><style face="superscript">6,10,11</style></DisplayText><record><rec-number>37</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">37</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Biostatistics and Epidemiology, Perelman School of Medicine, University of Pennsylvania, PA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>27</RecNum><record><rec-number>27</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">27</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Non-Communicable Diseases, Karachi, Pakistan</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>23</RecNum><record><rec-number>23</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">23</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}†, He Zhang{ HYPERLINK \l "_ENREF_12" \o ", #67" }, Ellen M. Schmidt{ HYPERLINK \l "_ENREF_13" \o ", #55" }, Lars Fritsche{ HYPERLINK \l "_ENREF_14" \o ", #17" }, Nathan Stitziel{ ADDIN EN.CITE <EndNote><Cite><RecNum>162</RecNum><DisplayText><style face="superscript">15,16</style></DisplayText><record><rec-number>162</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459878031">162</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Division, Departments of Medicine and Genetics, Washington University School of Medicine, St. Louis, MO, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>163</RecNum><record><rec-number>163</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459888015">163</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The McDonnell Genome Institute, Washington University School of Medicine, St. Louis, MO, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Franco Giulianini{ HYPERLINK \l "_ENREF_17" \o ", #87" }, Amit Khera{ ADDIN EN.CITE <EndNote><Cite><RecNum>26</RecNum><DisplayText><style

face="superscript">2,4</style></DisplayText><record><rec-number>26</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">26</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Connor Emdin{ ADDIN EN.CITE <EndNote><Cite><RecNum>26</RecNum><DisplayText><style face="superscript">2,4</style></DisplayText><record><rec-number>26</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">26</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Paul L. Auer{ HYPERLINK \l "_ENREF_18" \o ", #157" }, Peter E. Weeke{ ADDIN EN.CITE <EndNote><Cite><RecNum>72</RecNum><DisplayText><style face="superscript">19,20</style></DisplayText><record><rec-number>72</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">72</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>140</RecNum><record><rec-number>140</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">140</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Heart Centre, Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Alanna C. Morrison{ HYPERLINK \l "_ENREF_21" \o ", #102" }, Anette Varbo{ ADDIN EN.CITE <EndNote><Cite><RecNum>48</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>93</RecNum><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Xueling Sim{ ADDIN EN.CITE <EndNote><Cite><RecNum>17</RecNum><DisplayText><style

face="superscript">14,24</style></DisplayText><record><rec-number>17</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1446564249">17</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Statistical Genetics, Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>133</RecNum><record><rec-number>133</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">133</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Saw Swee Hock School of Public Health, National University of Singapore, Singapore, 117549, Singapore</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Ruth Frikke-Schmidt{ ADDIN EN.CITE <EndNote><Cite><RecNum>50</RecNum><DisplayText><style face="superscript">25,26</style></DisplayText><record><rec-number>50</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">50</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry, Rigshospitalet, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>92</RecNum><record><rec-number>92</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">92</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Ani Manichaikul{ HYPERLINK \l "_ENREF_27" \o ", #28" }, Yanhua Zhou{ HYPERLINK \l "_ENREF_3" \o ", #18" }, Marianne Benn{ ADDIN EN.CITE <EndNote><Cite><RecNum>48</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>93</RecNum><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Niels Grarup{ HYPERLINK \l "_ENREF_28" \o ", #146" }, Yingchang Lu{ HYPERLINK \l "_ENREF_29" \o ", #138" }, Yan Zhang{ HYPERLINK \l "_ENREF_30" \o ", #42" }, Giorgio Pistis{ HYPERLINK \l "_ENREF_31" \o ", #155" }, Alisa K. Manning{ ADDIN EN.CITE <EndNote><Cite><RecNum>19</RecNum><DisplayText><style face="superscript">2,4,32</style></DisplayText><record><rec-number>19</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1446564610">19</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Massachusetts General Hospital, Boston, MA, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>26</RecNum><record><rec-number>26</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">26</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for

Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Tõnu Esko{ ADDIN EN.CITE <EndNote><Cite><RecNum>156</RecNum><DisplayText><style face="superscript">4,33</style></DisplayText><record><rec-number>156</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459868450">156</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Estonian Genome Center, University of Tartu, Tartu, Estonia</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Joshua C. Bis{ HYPERLINK \l "_ENREF_34" \o ", #24" }, Aniruddh P. Patel{ ADDIN EN.CITE <EndNote><Cite><RecNum>70</RecNum><DisplayText><style face="superscript">2,4,35,36</style></DisplayText><record><rec-number>70</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">70</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Harvard Medical School, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>25</RecNum><record><rec-number>25</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">25</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>26</RecNum><record><rec-number>26</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">26</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Anne U Jackson{ HYPERLINK \l "_ENREF_14" \o ", #17" }, Li An Lin{ HYPERLINK \l "_ENREF_37" \o ", #111" }, Mary F Feitosa{ HYPERLINK \l "_ENREF_38" \o ", #89" }, Jette Bork-Jensen{ HYPERLINK \l "_ENREF_28" \o ", #146" }, Kathleen E Stirrups{ ADDIN EN.CITE <EndNote><Cite><RecNum>154</RecNum><DisplayText><style face="superscript">39,40</style></DisplayText><record><rec-number>154</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">154</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London,

UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>64</RecNum><record><rec-number>64</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">64</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Haematology, University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Hayato Tada{ HYPERLINK \l "_ENREF_41" \o ", #85" }, Johanna Jakobsdottir{ ADDIN EN.CITE <EndNote><Cite><RecNum>141</RecNum><DisplayText><style face="superscript">42,43</style></DisplayText><record><rec-number>141</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">141</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Icelandic Heart Association, Kopavogur, Iceland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>147</RecNum><record><rec-number>147</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">147</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The University of Iceland, Reykjavik, Iceland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Jennifer Huffman{ HYPERLINK \l "_ENREF_44" \o ", #116" }, Martina Müller-Nurasyid{ HYPERLINK \l "_ENREF_45" \o ", #68" }, Oddgeir L. Holmen{ ADDIN EN.CITE <EndNote><Cite><RecNum>79</RecNum><DisplayText><style face="superscript">48,49</style></DisplayText><record><rec-number>79</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">79</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Public Health and General Practice, HUNT Research Centre, Norwegian University of Science and Technology, 7600 Levanger, Norway</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>134</RecNum><record><rec-number>134</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">134</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>St Olav Hospital, Trondheim University Hospital, 7030 Trondheim, Norway</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Weihua Zhang{ HYPERLINK \l "_ENREF_50" \o ", #56" }, Helen R Warren{ HYPERLINK \l "_ENREF_51" \o ", #32" }, Johanne M. Justesen{ HYPERLINK \l "_ENREF_28" \o ", #146" }, Nicholas GD Masca{ ADDIN EN.CITE <EndNote><Cite><RecNum>46</RecNum><DisplayText><style face="superscript">52,53</style></DisplayText><record><rec-number>46</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">46</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiovascular Sciences, University of Leicester, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>123</RecNum><record><rec-number>123</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">123</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>NIHR Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Alexessander Couto Alves{ HYPERLINK \l "_ENREF_54" \o ", #105" }, Hanieh Yaghootkar{ HYPERLINK \l "_ENREF_55" \o ", #97" }, Ming Xu{ HYPERLINK \l "_ENREF_56" \o ", #40" }, Robert A. Scott{ HYPERLINK \l "_ENREF_57" \o ", #119" }, Heather M Stringham{ HYPERLINK \l

"_ENREF_14" \o ", #17" }, Wei Zhou{ HYPERLINK \l "_ENREF_13" \o ", #55" }, Gail Davies{ ADDIN EN.CITE <EndNote><Cite><RecNum>29</RecNum><DisplayText><style face="superscript">58,59</style></DisplayText><record><rec-number>29</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">29</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>77</RecNum><record><rec-number>77</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">77</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Psychology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Aliki-Eleni Farmaki{ HYPERLINK \l "_ENREF_60" \o ", #73" }, Neil R Robertson{ ADDIN EN.CITE <EndNote><Cite><RecNum>125</RecNum><DisplayText><style face="superscript">9,61</style></DisplayText><record><rec-number>125</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">125</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Oxford Centre for Diabetes, Endocrinology and Metabolism, Radcliffe Department of Medicine, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>152</RecNum><record><rec-number>152</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">152</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Frida Renström{ ADDIN EN.CITE <EndNote><Cite><RecNum>34</RecNum><DisplayText><style face="superscript">62,63</style></DisplayText><record><rec-number>34</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">34</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Biobank Research, Umeå University, Umeå, Sweden</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>54</RecNum><record><rec-number>54</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">54</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Sciences, Genetic and Molecular Epidemiology Unit, Lund University, Malmö, Sweden</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Tibor V Varga{ HYPERLINK \l "_ENREF_63" \o ", #54" }, Lorraine Southam{ ADDIN EN.CITE <EndNote><Cite><RecNum>152</RecNum><DisplayText><style face="superscript">9,64</style></DisplayText><record><rec-number>152</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">152</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>153</RecNum><record><rec-number>153</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">153</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Sanger Institute, Genome Campus, Hinxton,

UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Suthesh Sivapalaratnam{ HYPERLINK \l "_ENREF_65" \o ", #82" }, David CM Liewald{ ADDIN EN.CITE <EndNote><Cite><RecNum>29</RecNum><DisplayText><style face="superscript">58,59</style></DisplayText><record><rec-number>29</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">29</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>77</RecNum><record><rec-number>77</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">77</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Psychology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Christian M. Shaffer{ HYPERLINK \l "_ENREF_19" \o ", #72" }, Anne Langsted{ ADDIN EN.CITE <EndNote><Cite><RecNum>93</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>48</RecNum><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Stavroula Kanoni{ HYPERLINK \l "_ENREF_39" \o ", #154" }, Serena Sanna{ HYPERLINK \l "_ENREF_31" \o ", #155" }, Xiangfeng Lu{ ADDIN EN.CITE <EndNote><Cite><RecNum>67</RecNum><DisplayText><style face="superscript">12,66</style></DisplayText><record><rec-number>67</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">67</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Internal Medicine, Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan 48109, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>135</RecNum><record><rec-number>135</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">135</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Kent D Taylor{ HYPERLINK \l "_ENREF_67" \o ", #114" }, Dorota Pasko{ HYPERLINK \l "_ENREF_55" \o ", #97" }, Natalie R van Zuydam{ ADDIN EN.CITE <EndNote><Cite><RecNum>117</RecNum><DisplayText><style face="superscript">9,68</style></DisplayText><record><rec-number>117</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">117</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Medical Research Institute, University of Dundee,

Ninewells Hospital and Medical School, Dundee, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>152</RecNum><record><rec-number>152</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">152</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Robin Young{ HYPERLINK \l "_ENREF_6" \o ", #23" }, Praveen Surendran{ HYPERLINK \l "_ENREF_6" \o ", #23" }, Audrey Y. Chu{ ADDIN EN.CITE <EndNote><Cite><RecNum>87</RecNum><DisplayText><style face="superscript">17,69</style></DisplayText><record><rec-number>87</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">87</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Preventive Medicine, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>121</RecNum><record><rec-number>121</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">121</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>NHLBI Framingham Heart Study, Framingham, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Asif Rasheed{ HYPERLINK \l "_ENREF_11" \o ", #27" }, Sehrish Jabeen{ HYPERLINK \l "_ENREF_11" \o ", #27" }, Philippe Frossard{ HYPERLINK \l "_ENREF_11" \o ", #27" }, The EPIC-InterAct consortium, EPIC-CVD Consortium, Charge Diabetes Working Group, Jennifer Wessel{ ADDIN EN.CITE <EndNote><Cite><RecNum>174</RecNum><DisplayText><style face="superscript">70,71</style></DisplayText><record><rec-number>174</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471976846">174</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Epidemiology, Indiana University Fairbanks School of Public Health, Indianapolis, Indiana, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>175</RecNum><record><rec-number>175</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471976865">175</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Mark O. Goodarzi{ ADDIN EN.CITE <EndNote><Cite><RecNum>176</RecNum><DisplayText><style face="superscript">72,73</style></DisplayText><record><rec-number>176</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471977009">176</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine and Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California 90048, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>177</RecNum><record><rec-number>177</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471977026">177</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Endocrinology, Diabetes and Metabolism, Cedars-Sinai Medical Center, Los Angeles, California 90048, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Megan L. Grove{ HYPERLINK \l "_ENREF_21" \o ", #102" }, Antonella Mulas{ HYPERLINK \l "_ENREF_31" \o ", #155" }, Magdalena Zoledziewska{ HYPERLINK \l "_ENREF_31" \o ", #155" }, Fabio Busonero{ HYPERLINK \l "_ENREF_31" \o ", #155" }, Andrea Maschio{ HYPERLINK \l

"_ENREF_31" \o ", #155" }, Joel N. Hirschhorn{ ADDIN EN.CITE <EndNote><Cite><RecNum>178</RecNum><DisplayText><style face="superscript">4,74</style></DisplayText><record><rec-number>178</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471977221">178</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Endocrinology and Center for Basic and Translational Obesity Research, Boston Children's Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Reedik Mägi{ HYPERLINK \l "_ENREF_33" \o ", #156" }, Kari Kuulasmaa{ HYPERLINK \l "_ENREF_75" \o ", #65" }, Markus Perola{ ADDIN EN.CITE <EndNote><Cite><RecNum>65</RecNum><DisplayText><style face="superscript">75,76</style></DisplayText><record><rec-number>65</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">65</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Health, National Institute for Health and Welfare, FI-00271, Helsinki, Finland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>110</RecNum><record><rec-number>110</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">110</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Molecular Medicine FIMM, University of Helsinki, Finland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Veikko Salomaa{ HYPERLINK \l "_ENREF_75" \o ", #65" }, Philippe Amouyel{ HYPERLINK \l "_ENREF_77" \o ", #179" }, Dominique Arveiler{ HYPERLINK \l "_ENREF_78" \o ", #57" }, Cramer Christensen{ HYPERLINK \l "_ENREF_79" \o ", #115" }, Jean Ferrieres{ HYPERLINK \l "_ENREF_80" \o ", #59" }, Marco Ferrario{ HYPERLINK \l "_ENREF_81" \o ", #130" }, Frank Kee{ HYPERLINK \l "_ENREF_82" \o ", #83" }, Jarmo Virtamo{ HYPERLINK \l "_ENREF_75" \o ", #65" }, Marit E. Jørgensen{ ADDIN EN.CITE <EndNote><Cite><RecNum>136</RecNum><DisplayText><style face="superscript">83,84</style></DisplayText><record><rec-number>136</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">136</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Steno Diabetes Center, Gentofte, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>159</RecNum><record><rec-number>159</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459872340">159</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>National Institute of Public Health, Southern Denmark University, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Torsten Lauritzen{ HYPERLINK \l "_ENREF_85" \o ", #80" }, Ivan Brandslund{ ADDIN EN.CITE <EndNote><Cite><RecNum>49</RecNum><DisplayText><style face="superscript">86,87</style></DisplayText><record><rec-number>49</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">49</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry, Lillebaelt

Hospital, Vejle, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>112</RecNum><record><rec-number>112</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">112</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Rajiv Chowdhury{ HYPERLINK \l "_ENREF_6" \o ", #23" }, Emanuele di Angelantonio{ ADDIN EN.CITE <EndNote><Cite><RecNum>23</RecNum><DisplayText><style face="superscript">6,7</style></DisplayText><record><rec-number>23</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">23</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>145</RecNum><record><rec-number>145</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">145</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The National Institute for Health Research Blood and Transplant Unit (NIHR BTRU) in Donor Health and Genomics at the University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Dewar Alam{ HYPERLINK \l "_ENREF_88" \o ", #103" }, Erwin P. Bottinger{ HYPERLINK \l "_ENREF_29" \o ", #138" }, Ian Ford{ HYPERLINK \l "_ENREF_89" \o ", #150" }, Stella Trompet{ ADDIN EN.CITE <EndNote><Cite><RecNum>41</RecNum><DisplayText><style face="superscript">90,91</style></DisplayText><record><rec-number>41</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">41</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>63</RecNum><record><rec-number>63</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">63</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, the Netherlands</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Naveed Sattar{ HYPERLINK \l "_ENREF_92" \o ", #22" }, J. Wouter Jukema{ ADDIN EN.CITE <EndNote><Cite><RecNum>41</RecNum><DisplayText><style face="superscript">90,93</style></DisplayText><record><rec-number>41</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">41</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>143</RecNum><record><rec-number>143</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">143</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Heikki A. Koistinen{ ADDIN EN.CITE <EndNote><Cite><RecNum>65</RecNum><DisplayText><style face="superscript">75,94,95</style></DisplayText><record><rec-number>65</rec-number><foreign-

keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">65</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Health, National Institute for Health and Welfare, FI-00271, Helsinki, Finland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>190</RecNum><record><rec-number>190</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1483648585">190</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, and Abdominal Center: Endocrinology, Helsinki University Central Hospital, Helsinki, Finland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>191</RecNum><record><rec-number>191</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1483648621">191</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Minerva Foundation Institute for Medical Research, Helsinki, Finland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Morris Brown{ HYPERLINK \l "_ENREF_96" \o ", #165" }, Allan Linneberg{ HYPERLINK \l "_ENREF_97" \o ", #51" }, Charlotta Pisinger{ HYPERLINK \l "_ENREF_99" \o ", #129" }, Yii-Der Ida Chen{ HYPERLINK \l "_ENREF_100" \o ", #142" }, John M Connell{ HYPERLINK \l "_ENREF_68" \o ", #117" }, Anna Dominiczak{ HYPERLINK \l "_ENREF_92" \o ", #22" }, Gudny Eiriksdottir{ HYPERLINK \l "_ENREF_42" \o ", #141" }, Melissa E. Garcia{ HYPERLINK \l "_ENREF_101" \o ", #164" }, Harald Grallert{ ADDIN EN.CITE <EndNote><Cite><RecNum>98</RecNum><DisplayText><style face="superscript">47,102,103</style></DisplayText><record><rec-number>98</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">98</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>German Center for Diabetes Research (DZD e.V.), Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>108</RecNum><record><rec-number>108</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">108</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Genetic Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>131</RecNum><record><rec-number>131</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">131</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Research Unit of Molecular Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Tamara B. Harris{ HYPERLINK \l "_ENREF_101" \o ", #164" }, Lenore J. Launer{ HYPERLINK \l "_ENREF_101" \o ", #164" }, Eirini Marouli{ HYPERLINK \l "_ENREF_39" \o ", #154" }, Matt J Neville{ HYPERLINK \l "_ENREF_61" \o ", #125" }, Annette Peters{ ADDIN EN.CITE <EndNote><Cite><RecNum>90</RecNum><DisplayText><style face="superscript">46,47,102</style></DisplayText><record><rec-number>90</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">90</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>DZHK German Centre for Cardiovascular Research, Munich,

Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>98</RecNum><record><rec-number>98</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">98</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>German Center for Diabetes Research (DZD e.V.), Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>108</RecNum><record><rec-number>108</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">108</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Genetic Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Neil Poulter{ HYPERLINK \l "_ENREF_104" \o ", #167" }, Peter Sever{ HYPERLINK \l "_ENREF_104" \o ", #167" }, Kerrin S Small{ HYPERLINK \l "_ENREF_105" \o ", #81" }, Albert V. Smith{ ADDIN EN.CITE <EndNote><Cite><RecNum>141</RecNum><DisplayText><style face="superscript">42,43</style></DisplayText><record><rec-number>141</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">141</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Icelandic Heart Association, Kopavogur, Iceland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>147</RecNum><record><rec-number>147</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">147</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The University of Iceland, Reykjavik, Iceland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Melanie Waldenberger{ ADDIN EN.CITE <EndNote><Cite><RecNum>108</RecNum><DisplayText><style face="superscript">47,103</style></DisplayText><record><rec-number>108</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">108</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Genetic Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>131</RecNum><record><rec-number>131</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">131</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Research Unit of Molecular Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Timo Lakka{ ADDIN EN.CITE <EndNote><Cite><RecNum>76</RecNum><DisplayText><style face="superscript">106,107</style></DisplayText><record><rec-number>76</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">76</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Physiology, Institute of Biomedicine, University of Eastern Finland, Kuopio Campus, Kuopio, Finland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>113</RecNum><record><rec-number>113</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">113</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Kuopio Research Institute of Exercise Medicine, Kuopio, Finland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Igor Rudan{

HYPERLINK \l "_ENREF_108" \o ", #151" }, Pekka Mäntyselkä{ HYPERLINK \l "_ENREF_109" \o ", #61" }, John C Chambers{ ADDIN EN.CITE <EndNote><Cite><RecNum>56</RecNum><DisplayText><style face="superscript">50,110,111</style></DisplayText><record><rec-number>56</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">56</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Norfolk Place, London W2 1PG, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>39</RecNum><record><rec-number>39</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">39</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiology, Ealing Hospital NHS Trust, Uxbridge Road, Southall, Middlesex UB1 3HW, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>160</RecNum><record><rec-number>160</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459873607">160</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Imperial College Healthcare NHS Trust, London, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Colin NA Palmer{ HYPERLINK \l "_ENREF_68" \o ", #117" }, Francesco Cucca{ ADDIN EN.CITE <EndNote><Cite><RecNum>155</RecNum><DisplayText><style face="superscript">31,112</style></DisplayText><record><rec-number>155</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459868421">155</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Istituto di Ricerca Genetica e Biomedica, Consiglio Nazionale delle Ricerche (CNR), Monserrato, Cagliari, Italy</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>168</RecNum><record><rec-number>168</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1462479234">168</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Dipartimento di Scienze Biomediche, Universita' degli Studi di Sassari, Sassari, Italy</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Leif Groop{ HYPERLINK \l "_ENREF_113" \o ", #170" }, Andres Metspalu{ HYPERLINK \l "_ENREF_33" \o ", #156" }, Y. Eugene Chen{ HYPERLINK \l "_ENREF_12" \o ", #67" }, Lia E. Bang{ HYPERLINK \l "_ENREF_114" \o ", #44" }, Marie-Pierre Dubé{ HYPERLINK \l "_ENREF_115" \o ", #118" }, John D. Rioux{ HYPERLINK \l "_ENREF_115" \o ", #118" }, Sandosh Padmanabhan{ HYPERLINK \l "_ENREF_92" \o ", #22" }, Blair H Smith{ ADDIN EN.CITE <EndNote><Cite><RecNum>86</RecNum><DisplayText><style face="superscript">118,119</style></DisplayText><record><rec-number>86</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">86</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Population Health Sciences, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>96</RecNum><record><rec-number>96</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">96</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Generation Scotland, Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Jose M. Ordovas{

HYPERLINK \l "_ENREF_120" \o ", #45" }, Torben Hansen{ ADDIN EN.CITE <EndNote><Cite><RecNum>94</RecNum><DisplayText><style face="superscript">28,123</style></DisplayText><record><rec-number>94</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">94</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>146</RecNum><record><rec-number>146</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">146</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Gorm B Jensen{ HYPERLINK \l "_ENREF_124" \o ", #139" }, Johanna Kuusisto{ HYPERLINK \l "_ENREF_125" \o ", #107" }, Pia R. Kamstrup{ ADDIN EN.CITE <EndNote><Cite><RecNum>48</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>93</RecNum><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Christie M. Ballantyne{ HYPERLINK \l "_ENREF_126" \o ", #69" }, Neil S. Zheng{ HYPERLINK \l "_ENREF_127" \o ", #181" }, Joshua C. Denny{ ADDIN EN.CITE <EndNote><Cite><RecNum>35</RecNum><DisplayText><style face="superscript">19,128</style></DisplayText><record><rec-number>35</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">35</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>72</RecNum><record><rec-number>72</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">72</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Charles L. Kooperberg{ HYPERLINK \l "_ENREF_129" \o ", #88" }, Hua Tang{ HYPERLINK \l "_ENREF_130" \o ", #62" }, Anders Malarstig{ ADDIN EN.CITE <EndNote><Cite><RecNum>188</RecNum><DisplayText><style face="superscript">131,132</style></DisplayText><record><rec-number>188</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1473727341">188</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Genetics and Genomics Group, Cardiovascular Medicine Unit, Department of Medicine, Solna, Karolinska Institutet, Stockholm,

Sweden</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>189</RecNum><record><rec-number>189</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1473727380">189</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Pharmatherapeutics Clinical Research, Pfizer Worldwide R&D, Sollentuna, Sweden</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Dermot Reilly{ HYPERLINK \l "_ENREF_133" \o ", #187" }, Paul M Ridker{ HYPERLINK \l "_ENREF_17" \o ", #87" }, Jaakko Tuomilehto{ HYPERLINK \l "_ENREF_134" \o ", #31" }, John M Starr{ ADDIN EN.CITE <EndNote><Cite><RecNum>29</RecNum><DisplayText><style face="superscript">58,138</style></DisplayText><record><rec-number>29</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">29</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>20</RecNum><record><rec-number>20</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">20</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Alzheimer Scotland Dementia Research Centre, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Rainer Raumaraa{ ADDIN EN.CITE <EndNote><Cite><RecNum>53</RecNum><DisplayText><style face="superscript">107,139</style></DisplayText><record><rec-number>53</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">53</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>113</RecNum><record><rec-number>113</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">113</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Kuopio Research Institute of Exercise Medicine, Kuopio, Finland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Patricia B. Munroe{ ADDIN EN.CITE <EndNote><Cite><RecNum>32</RecNum><DisplayText><style face="superscript">51,140</style></DisplayText><record><rec-number>32</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">32</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Clinical Pharmacology, William Harvey Research Institute, Barts and The London, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>122</RecNum><record><rec-number>122</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">122</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>NIHR Barts Cardiovascular Biomedical Research Unit, Queen Mary University of London, London, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Eleftheria Zeggini{ HYPERLINK \l "_ENREF_64" \o ", #153" }, Ozren Polasek{ ADDIN EN.CITE <EndNote><Cite><RecNum>95</RecNum><DisplayText><style face="superscript">108,141</style></DisplayText><record><rec-number>95</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs"

timestamp="1459711619">95</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Medicine, University of Split, Split, Croatia</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>151</RecNum><record><rec-number>151</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">151</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>**}**, Paul W. Franks**{** ADDIN EN.CITE <EndNote><Cite><RecNum>54</RecNum><DisplayText><style face="superscript">63,142,143</style></DisplayText><record><rec-number>54</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">54</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Sciences, Genetic and Molecular Epidemiology Unit, Lund University, Malmö, Sweden</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>78</RecNum><record><rec-number>78</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">78</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Public Health & Clinical Medicine, Umeå University, Umeå, Sweden</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>161</RecNum><record><rec-number>161</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459875684">161</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>**}**, Timothy D Spector**{** HYPERLINK \l "_ENREF_105" \o ", #81" **}**, George Dedoussis**{** HYPERLINK \l "_ENREF_60" \o ", #73" **}**, Ian J Deary**{** ADDIN EN.CITE <EndNote><Cite><RecNum>29</RecNum><DisplayText><style face="superscript">58,59</style></DisplayText><record><rec-number>29</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">29</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>77</RecNum><record><rec-number>77</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">77</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Psychology, University of Edinburgh, Edinburgh, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>**}**, Santhi K. Ganesh**{** ADDIN EN.CITE <EndNote><Cite><RecNum>67</RecNum><DisplayText><style face="superscript">12,144</style></DisplayText><record><rec-number>67</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">67</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Internal Medicine, Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan 48109, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>66</RecNum><record><rec-number>66</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">66</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Human Genetics, University of Michigan, Ann Arbor, Michigan 48109,

USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Claudia Langenberg{ HYPERLINK \l "_ENREF_57" \o ", #119" }, Nick J. Wareham{ HYPERLINK \l "_ENREF_57" \o ", #119" }, Wei Gao{ HYPERLINK \l "_ENREF_145" \o ", #43" }, Timothy M. Frayling{ HYPERLINK \l "_ENREF_55" \o ", #97" }, Marjo-Riitta Jarvelin{ HYPERLINK \l "_ENREF_54" \o ", #105" }, Nilesh J Samani{ ADDIN EN.CITE <EndNote><Cite><RecNum>46</RecNum><DisplayText><style face="superscript">52,53</style></DisplayText><record><rec-number>46</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">46</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiovascular Sciences, University of Leicester, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>123</RecNum><record><rec-number>123</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">123</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>NIHR Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Andrew P Morris{ ADDIN EN.CITE <EndNote><Cite><RecNum>38</RecNum><DisplayText><style face="superscript">9,146</style></DisplayText><record><rec-number>38</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">38</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Biostatistics, University of Liverpool, Liverpool, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>152</RecNum><record><rec-number>152</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">152</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, James G. Wilson{ HYPERLINK \l "_ENREF_147" \o ", #75" }, Mark J Caulfield{ ADDIN EN.CITE <EndNote><Cite><RecNum>32</RecNum><DisplayText><style face="superscript">51,148</style></DisplayText><record><rec-number>32</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">32</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Clinical Pharmacology, William Harvey Research Institute, Barts and The London, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>137</RecNum><record><rec-number>137</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">137</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Barts Heart Centre, William Harvey Research Institute, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Tapani Ebeling{ HYPERLINK \l "_ENREF_149" \o ", #71" }, Jaspal S Kooner{ ADDIN EN.CITE <EndNote><Cite><RecNum>120</RecNum><DisplayText><style face="superscript">110,111,150</style></DisplayText><record><rec-number>120</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">120</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>National Heart and Lung Institute, Imperial College London, Hammersmith Hospital Campus, London,

UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>120</RecNum><record><rec-number>120</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">120</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>National Heart and Lung Institute, Imperial College London, Hammersmith Hospital Campus, London, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>160</RecNum><record><rec-number>160</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459873607">160</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Imperial College Healthcare NHS Trust, London, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>39</RecNum><record><rec-number>39</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">39</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Cardiology, Ealing Hospital NHS Trust, Uxbridge Road, Southall, Middlesex UB1 3HW, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Kristian Hveem{ HYPERLINK \l "_ENREF_48" \o ", #79" }, Christian Gieger{ ADDIN EN.CITE <EndNote><Cite><RecNum>98</RecNum><DisplayText><style face="superscript">47,102,103</style></DisplayText><record><rec-number>98</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">98</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>German Center for Diabetes Research (DZD e.V.), Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>108</RecNum><record><rec-number>108</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">108</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Genetic Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>131</RecNum><record><rec-number>131</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">131</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Research Unit of Molecular Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Konstantin Strauch{ ADDIN EN.CITE <EndNote><Cite><RecNum>108</RecNum><DisplayText><style face="superscript">47,151</style></DisplayText><record><rec-number>108</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">108</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Genetic Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>109</RecNum><record><rec-number>109</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">109</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Institute of Medical Informatics, Biometry and Epidemiology, Chair of Genetic Epidemiology, Ludwig-Maximilians-Universität, Munich, Germany</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Vilmundur Gudnason{ ADDIN EN.CITE <EndNote><Cite><RecNum>141</RecNum><DisplayText><style face="superscript">42,43</style></DisplayText><record><rec-number>141</rec-number><foreign-

keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">141</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Icelandic Heart Association, Kopavogur, Iceland</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>147</RecNum><record><rec-number>147</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">147</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The University of Iceland, Reykjavik, Iceland</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Myriam Fornage{ HYPERLINK \l "_ENREF_37" \o ", #111" }, Daniel J. Rader{ ADDIN EN.CITE <EndNote><Cite><RecNum>185</RecNum><DisplayText><style face="superscript">152,153</style></DisplayText><record><rec-number>185</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1472487088">185</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>186</RecNum><record><rec-number>186</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1472487105">186</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Michael Boehnke{ HYPERLINK \l "_ENREF_14" \o ", #17" }, Marju Orho-Melander{ HYPERLINK \l "_ENREF_154" \o ", #182" }, Olle Melander{ HYPERLINK \l "_ENREF_154" \o ", #182" }, Fredrik Karpe{ ADDIN EN.CITE <EndNote><Cite><RecNum>125</RecNum><DisplayText><style face="superscript">61,155</style></DisplayText><record><rec-number>125</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">125</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Oxford Centre for Diabetes, Endocrinology and Metabolism, Radcliffe Department of Medicine, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>126</RecNum><record><rec-number>126</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">126</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Oxford NIHR Biomedical Research Centre, Oxford University Hospitals Trust, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Bruce M. Psaty{ ADDIN EN.CITE <EndNote><Cite><RecNum>24</RecNum><DisplayText><style face="superscript">34,156,157</style></DisplayText><record><rec-number>24</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">24</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>100</RecNum><record><rec-number>100</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">100</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Group Health Research Institute, Group Health Cooperative, Seattle, WA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>184</RecNum><record><rec-number>184</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1472227392">184</key></foreign-keys><ref-

type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Departments of Epidemiology and Health Services, University of Washington, Seattle, WA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Yong Huo{ HYPERLINK \l "_ENREF_30" \o ", #42" }, Ruth J.F. Loos{ ADDIN EN.CITE <EndNote><Cite><RecNum>138</RecNum><DisplayText><style face="superscript">29,158</style></DisplayText><record><rec-number>138</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">138</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Charles Bronfman Institute for Personalized Medicine, Ichan School of Medicine at Mount Sinai, New York, NY 10029, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>144</RecNum><record><rec-number>144</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">144</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The Mindich Child Health and Development Institute, Ichan School of Medicine at Mount Sinai, New York, NY 10029, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Oluf Pedersen{ HYPERLINK \l "_ENREF_28" \o ", #146" }, Sune F Nielsen{ ADDIN EN.CITE <EndNote><Cite><RecNum>48</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>93</RecNum><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Jean-Claude Tardif{ ADDIN EN.CITE <EndNote><Cite><RecNum>118</RecNum><DisplayText><style face="superscript">115,117</style></DisplayText><record><rec-number>118</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">118</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Montreal Heart Institute, Montreal, Quebec, Canada</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>149</RecNum><record><rec-number>149</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">149</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Université de Montréal, Montreal, Quebec, Canada</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Caroline Hayward{ HYPERLINK \l "_ENREF_44" \o ", #116" }, L. Adrienne Cupples{ ADDIN EN.CITE <EndNote><Cite><RecNum>18</RecNum><DisplayText><style face="superscript">3,69</style></DisplayText><record><rec-number>18</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1446564580">18</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>121</RecNum><record><rec-number>121</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">121</key></foreign-keys><ref-

type name="Journal Article">17</ref-type><contributors></contributors><titles><title>NHLBI Framingham Heart Study, Framingham, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Jerome I. Rotter{ HYPERLINK \l "_ENREF_100" \o ", #142" }, Stephen S Rich{ HYPERLINK \l "_ENREF_27" \o ", #28" }, Anne Tybjaerg-Hansen{ ADDIN EN.CITE <EndNote><Cite><RecNum>50</RecNum><DisplayText><style face="superscript">25,26</style></DisplayText><record><rec-number>50</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">50</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry, Rigshospitalet, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>92</RecNum><record><rec-number>92</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">92</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Markku Laakso{ HYPERLINK \l "_ENREF_125" \o ", #107" }, James B. Meigs{ ADDIN EN.CITE <EndNote><Cite><RecNum>128</RecNum><DisplayText><style face="superscript">4,32,159</style></DisplayText><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>19</RecNum><record><rec-number>19</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1446564610">19</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Massachusetts General Hospital, Boston, MA, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>171</RecNum><record><rec-number>171</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1469200721">171</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title> Division of General Internal Medicine, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Børge G Nordestgaardrk{ ADDIN EN.CITE <EndNote><Cite><RecNum>48</RecNum><DisplayText><style face="superscript">22,23</style></DisplayText><record><rec-number>48</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">48</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev and Gentofte Hospital, Copenhagen University Hospital, Denmark</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>93</RecNum><record><rec-number>93</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">93</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Faculty of Health and Medical Sciences, University of Denmark, Denmark</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Eric Boerwinkle{ HYPERLINK \l "_ENREF_21" \o ", #102" }, Dan M. Roden{ HYPERLINK \l "_ENREF_19" \o ", #72" }, Alex P. Reiner{ ADDIN EN.CITE <EndNote><Cite><RecNum>60</RecNum><DisplayText><style

face="superscript">129,160</style></DisplayText><record><rec-number>60</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">60</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Epidemiology, University of Washington, Seattle WA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>88</RecNum><record><rec-number>88</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">88</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle WA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Daniel I. Chasman{ ADDIN EN.CITE <EndNote><Cite><RecNum>87</RecNum><DisplayText><style face="superscript">17,161</style></DisplayText><record><rec-number>87</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">87</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Division of Preventive Medicine, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>101</RecNum><record><rec-number>101</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">101</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Harvard Medical School, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}, Joanna MM Howson{ HYPERLINK \l "_ENREF_6" \o ", #23" }[†], John Danesh{ ADDIN EN.CITE <EndNote><Cite><RecNum>23</RecNum><DisplayText><style face="superscript">6,7,64</style></DisplayText><record><rec-number>23</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">23</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>145</RecNum><record><rec-number>145</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">145</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>The National Institute for Health Research Blood and Transplant Unit (NIHR BTRU) in Donor Health and Genomics at the University of Cambridge, Cambridge, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>153</RecNum><record><rec-number>153</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">153</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Sanger Institute, Genome Campus, Hinxton, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†], Mark I McCarthy{ ADDIN EN.CITE <EndNote><Cite><RecNum>125</RecNum><DisplayText><style face="superscript">9,61,155</style></DisplayText><record><rec-number>125</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">125</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Oxford Centre for Diabetes, Endocrinology and Metabolism, Radcliffe Department of Medicine, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>126</RecNum><record><rec-number>126</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">126</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Oxford NIHR Biomedical Research Centre, Oxford University Hospitals Trust, Oxford,

UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>152</RecNum><record><rec-number>152</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">152</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†], Chad Cowan{ ADDIN EN.CITE <EndNote><Cite><RecNum>183</RecNum><DisplayText><style face="superscript">5,162</style></DisplayText><record><rec-number>183</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471981105">183</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Regenerative Medicine, Massachusetts General Hospital, Boston, MA 02114, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>172</RecNum><record><rec-number>172</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1471975580">172</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Stem Cell and Regenerative Biology, Harvard Stem Cell Institute, Harvard University, Cambridge, MA 02138, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†], Goncalo Abecasis{ HYPERLINK \l "_ENREF_14" \o ", #17" }[†], Panos Deloukas{ ADDIN EN.CITE <EndNote><Cite><RecNum>154</RecNum><DisplayText><style face="superscript">39,163</style></DisplayText><record><rec-number>154</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">154</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>127</RecNum><record><rec-number>127</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">127</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Princess Al-Jawhara Al-Brahim Centre of Excellence in Research of Hereditary Disorders (PACER-HD), King Abdulaziz University, Jeddah 21589, Saudi Arabia</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†], Kiran Musunuru{ HYPERLINK \l "_ENREF_8" \o ", #173" }[†], Cristen J. Willer{ ADDIN EN.CITE <EndNote><Cite><RecNum>55</RecNum><DisplayText><style face="superscript">12,13,144</style></DisplayText><record><rec-number>55</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">55</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan 48109, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>66</RecNum><record><rec-number>66</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">66</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Human Genetics, University of Michigan, Ann Arbor, Michigan 48109, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>67</RecNum><record><rec-number>67</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">67</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Internal Medicine, Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan 48109, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†]*, Sekar

Kathiresan{ ADDIN EN.CITE <EndNote><Cite><RecNum>25</RecNum><DisplayText><style face="superscript">2,4,35,36</style></DisplayText><record><rec-number>25</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">25</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA, USA.</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>26</RecNum><record><rec-number>26</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">26</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>70</RecNum><record><rec-number>70</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711618">70</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Department of Medicine, Harvard Medical School, Boston, MA, USA</title></titles><dates></dates><urls></urls></record></Cite><Cite><RecNum>128</RecNum><record><rec-number>128</rec-number><foreign-keys><key app="EN" db-id="sdxztdswq9p2axeext2vzttcffr0a0rwx9xs" timestamp="1459711619">128</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors></contributors><titles><title>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA</title></titles><dates></dates><urls></urls></record></Cite></EndNote>}[†]*

{ ADDIN EN.REFLIST **}**

†These authors contributed equally.

*Correspondence to:

Cristen Willer, cristen@umich.edu

Sekar Kathiresan, SKATHIRESAN1@mgh.harvard.edu

Plasma lipid levels are modifiable risk factors for atherosclerotic cardiovascular disease. In >300,000 participants, we screened DNA sequence variants on an exome-focused array for association with plasma lipids. Here, we identified 444 independent variants in 250 loci significantly associated with total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and/or triglycerides (TG), with 75 loci showing significant association with lipid traits for the first time. At one new gene for plasma TG (*A1CF* encoding APOBEC1 complementation factor), we used CRISPR-Cas9 genome editing to show that mice knocked-in for p.Gly398Ser displayed higher plasma TG, a pattern consistent with the human genetic data. Finally, we used variants to anticipate the clinical effects of lipid-modifying therapies and identify a gene – lipoprotein lipase – that lowers risks for both coronary artery disease and type 2 diabetes.

Main Text

Association studies testing common DNA sequence variation have uncovered 175 genetic loci that affect lipid levels in the population**{** HYPERLINK \l "_ENREF_1" \o "Teslovich, 2010 #1" **}**, with most variants residing in the non-coding portion of the genome. These findings have informed underlying lipid biology and elucidated the causal roles of lipid levels on cardiovascular disease**{** HYPERLINK \l "_ENREF_8" \o "Musunuru, 2010 #8" **}**. Here, we build on these previous efforts to: 1) perform an exome-wide association screen for plasma lipids in >300,000 individuals; 2) evaluate a discovered allele *in vitro* and *in vivo* using CRISPR-Cas9 editing; and 3) test the inter-relationship of mapped lipid variants with three diseases – age-related macular degeneration (AMD), coronary artery disease (CAD), and type 2 diabetes mellitus.

We tested the association of genotypes from the HumanExome BeadChip (or exome array) with lipid levels in each of 73 studies encompassing >300,000 participants (Supplementary Material, Tables S1-S3). A total of 242,289 variants were analyzed after quality control (Supplementary Methods). A majority of the genotyped variants are non-synonymous with minor allele frequency (MAF) < 0.1% (Table S4). Single-variant association statistics and inter-marker linkage disequilibrium information summarized across 1 megabase sliding windows were generated from each cohort using RAREMETALWORKER or RVTESTS**{** ADDIN EN.CITE **{** ADDIN EN.CITE.DATA **}}** software. Meta-analyses of genetic associations were performed using the R-package rareMETALS (version 6.0).

In addition to testing each variant individually for association, we also performed gene-level association tests, which aggregate multiple rare coding variants in each of 16,798 protein-coding genes. Genomic control values for meta-analysis results were between 1.09 and 1.14 for all four lipid traits (Fig. S1), suggesting that population structure in our analysis is well-controlled**{** ADDIN EN.CITE **{** ADDIN EN.CITE.DATA **}{** ADDIN EN.CITE.DATA **}{** ADDIN EN.CITE.DATA **}}**.

In single-variant association analyses, we identified 1,445 variants associated at $P < 2.1 \times 10^{-7}$ (Bonferroni correction of 242,289 variants analyzed) (full association results will be made available with publication). Of these, 75 were 'novel', i.e., located in previously unreported loci: 35 of these were protein-altering variants and 40 were non-coding variants (**Table 1**) (Table S5 & S6). These 75 new loci are each located at least 1 megabase from previously reported genome-wide association study (GWAS) signals (Table S7). The lead variant was common (MAF > 5%) in 61 of these 75 loci. Gene-level association analyses revealed an additional five genes where the signal was driven by multiple rare variants ($P < 4.2 \times 10^{-7}$, Bonferroni correction threshold for performing 5 tests on ~20,000 genes, Table S8).

At any given genetic locus, multiple coding and non-coding variants may contribute to plasma lipid levels in an independent fashion. We quantified this phenomenon by iteratively performing association analyses conditional on the top variants at all lipid loci (175 previously identified and 75 newly identified). With this procedure, we identified 444 variants independently associated with one or more of the four lipid traits (Fig. S2; Table S9). Collectively, these 444 variants explain 9%-12% of the overall phenotypic variance for plasma lipid levels; previously mapped variants had explained about 5%-9% of the variance.

The identification of lipid-associated coding variants using the exome array may help refine association signals at previously identified GWAS loci. We were able to evaluate this possibility in 131 of the 175 previously reported GWAS loci where the index variant or a proxy was available on the exome array, and associated with lipids levels with $P < 2.1 \times 10^{-7}$ (Table S10 and Table S11). For example, rs11136341, an intronic SNP close to the *PLEC* gene reported to be associated with LDL-C, was the original lead SNP in its GWAS locus ($P = 2 \times 10^{-13}$). In the current study, a protein-altering variant in *PARP10* is the top variant in the same locus (rs11136343; Leu395Pro; $P = 7 \times 10^{-26}$). After conditioning on *PARP10* Leu395Pro, the evidence for rs11136341 diminished ($P = 0.02$); in contrast, *PARP10* Leu395Pro remained significant ($P = 9 \times 10^{-13}$) after conditioning on rs11136341. *PARP10* has been shown to affect the hepatic secretion of apolipoprotein B (apoB) in human hepatocytes{ HYPERLINK \l

"_ENREF_15" \o "Shen, 2012 #15" **}**; these results suggest that *PARP10* may be the causal gene at this locus.

The emergence of genome-editing tools such as CRISPR-Cas9 has made it feasible to interrogate genes or variants both *in vitro* and *in vivo*. This approach holds particular appeal in following up the results of our exome array analysis, in which hundreds of protein-altering variants were robustly associated with circulating lipids.

For example, one of the strongest novel associations to emerge from genetic analyses was between *A1CF* p.Gly398Ser and TG [0.10-standard deviation (SD) increase in TG per copy of alternate allele, $P = 4 \times 10^{-11}$]; this rare variant (MAF = 0.7%) was also associated with increased circulating TC ($P = 4 \times 10^{-7}$) and nominally associated with increased risk of CAD (OR 1.12; $P = 0.02$). *A1CF* encodes APOBEC1 complementation factor, an RNA-binding protein which facilitates the RNA-editing action of APOBEC1 on the *APOB* transcript**{** ADDIN EN.CITE **{** ADDIN EN.CITE.DATA **}}**. We performed CRISPR-Cas9 deletion, rescue, and knock-in experiments to assess whether *A1CF* p.Gly398Ser is a causal mutation that alters TG metabolism.

CRISPR-Cas9-induced deletion of *A1CF* led to 72% and 65% reduction in secreted APOB100 compared to control cells in Huh7 and HepG2 human hepatoma cells, respectively (**Fig. 1A-1C;** Fig. S3). These findings are consistent with previous studies in rat primary hepatocytes that also showed significantly decreased apoB secretion after RNAi-based depletion of *A1CF***{ HYPERLINK \l "_ENREF_18" \o "Galloway, 2010 #18" *}***. A subsequent "rescue" experiment involving overexpression of wild-type or p.Gly398Ser A1CF in Huh7 cells with or without endogenous A1CF expression confirmed that significantly more APOB100 secretion was noted in cell lines expressing p.Gly398Ser A1CF (**Fig. 1D**).

We sought to further validate the A1CF gene and the p.Gly398Ser variant through the use of CRISPR-Cas9 to generate knock-in mice. Using a guide RNA targeting A1cf exon 9, the site of the codon for p.Gly398, and a 162-nucleotide single-strand DNA oligonucleotide repair

template containing the p.Gly398Ser variant as well as extra synonymous changes to prevent re-cleavage by CRISPR-Cas9, we generated mice of the C57BL/6J inbred background with an A1cfGly398Ser allele (hereafter referred to as KI) (**Fig. S4A, S4B**). We bred the KI allele to homozygosity and found that KI/KI mice were viable and healthy. We compared wild-type and KI/KI colony mates (n = 9, 8) with respect to TG levels (**Fig. S4C**). We found that KI/KI mice had 46% increased TG compared to wild-type mice (P = 0.05). In sum, these results indicate that A1CF is a causal gene for TG in humans and that the p.Gly398Ser variant is a causal mutation, with possible relevance to CAD.

DNA sequence variants in therapeutic target genes may prove useful in anticipating the efficacy and safety of pharmacologic modulation. Specifically, we addressed three questions relevant to the development of lipid-modifying medicines.

First, will CETP inhibitors being developed to raise HDL-C and lower coronary artery disease (CAD) risk lead to an adverse increased risk of age-related macular degeneration (AMD), a leading cause of blindness around the world? This question is motivated by the fact that earlier work had identified variants in several HDL-C genes as associated with AMD risk**{** ADDIN EN.CITE **{** ADDIN EN.CITE.DATA **}}**. We tested the association of each independent HDL-C variant with AMD risk. Across 168 independent HDL-C variants with MAF > 1%, the effect size of variant on HDL-C was positively correlated with its effect on AMD risk (correlation in effect sizes, $r = 0.41$, $P = 4.4\times 10^{-8}$; Table S12). However, there was evidence that this effect was driven by the 10 independent HDL-C associated variants in the CETP gene (heterogeneity across the different HDL-C-raising mechanisms ($\tau^2 = 0.91$, $P_{het} = 1.8 \times 10^{-15}$) (Table S13). A one-SD increase in HDL-C via a genetic risk score of the 10 *CETP* variants robustly associated with increased AMD risk (OR = 2.01, 95% CI = 1.88-2.14, 16,144 AMD cases, 17,832 controls, $P = 3.4\times10^{-97}$). When these 10 *CETP* variants were removed, there was no longer a relationship between genetically-altered HDL-C and AMD risk ($P = 0.17$). These genetic results suggest that raising HDL via CETP inhibition will increase the risk of AMD.

Second, will lowering LDL-C with lipid-modifying medicines always increase risk for type 2 diabetes? This question is motivated by the fact that in randomized controlled trials, statin therapy, a single mechanism of lowering LDL-C, increases risk for type 2 diabetes({ HYPERLINK "imap://sekar@imap.broadinstitute.org:993/fetch%3EUID%3E/INBOX/GLGC%20co-author%20feedback%3E48" \l "_ENREF_21" \o "Sattar, 2010 #747" }, { HYPERLINK "imap://sekar@imap.broadinstitute.org:993/fetch%3EUID%3E/INBOX/GLGC%20co-author%20feedback%3E48" \l "_ENREF_22" \o "Swerdlow, 2015 #746" }). We identified genetic evidence for five other mechanisms by which LDL-C lowering may increase the risk of type 2 diabetes. Of the 113 independent LDL-C variants, five (those at *TM6SF2* p.Glu167Lys, *APOE* chr19:4510002, *HNF4A* p.Thr136Ile, *PNPLA3* p.Ile148Met, and *GCKR* p.Leu446Pro) had the most compelling evidence for association, with the LDL-C lowering allele associated with *increased* risk for type 2 diabetes ($P < 4.0 \times 10^{-4}$ for each, Bonferroni correction threshold for performing tests at 113 variants, Table S14).

We further investigated one therapeutic target - *PCSK9* - as inhibitors of PCSK9 have been recently developed and it is uncertain if these medicines will increase risk for type 2 diabetes. Of 9 independent variants at the *PCSK9* locus associated with plasma LDL-C, R46L (2% frequency) explains the greatest proportion of LDL-C variance. A recent publication demonstrated that the L allele, linked to an ~16 mg/dl decrease in LDL-C, was associated with a 22% reduction in risk of CAD { HYPERLINK \l "_ENREF_21" \o "Myocardial Infarction, 2016 #21" }. Here, we evaluated the association of R46L on risk for type 2 diabetes among 222,877 participants. We found that the L46 allele associated with lower LDL-C confers a 13% increased risk for type 2 diabetes (OR 1.13; 95% CI 1.06 – 1.20; $P=6.96 \times 10^{-5}$) (**Fig. 2**). These genetic results are consistent with recent publications { HYPERLINK \l "_ENREF_22" \o "Lotta, 2016 #25" } and raise the possibility that lowering LDL via PCSK9 inhibition will reduce risk for CAD but increase risk of type 2 diabetes.

Finally, will modifying lipoprotein lipase (LPL) pathway activity simultaneously lower risk for both CAD and type 2 diabetes? Because modulation of LPL activity in oxidative tissues affects free fatty acid delivery**{** HYPERLINK \l "_ENREF_25" \o "Wang, 2015 #22" **}**, and thereby nutrient partitioning and insulin sensitivity, endogenous regulators of LPL activity may impact glycemic control and risk for development of type 2 diabetes. Using independent variants at six genes (*LPL* and five endogenous facilitators and inhibitors of LPL), we evaluated the effect of one standard deviation (SD) genetically-lowered TG on CAD and type 2 diabetes (Table S15). Variation in one gene - *LPL* – affected risk for both CAD and type 2 diabetes (Table S15). A one-SD decrease in TG mediated by *LPL* variants was associated with a 34% reduction in risk of CAD ($P = 4 \times 10^{-23}$) and a 20% reduction in risk of type 2 diabetes ($P = 0.0002$).

We sought to confirm this observation using a phenome-wide association study approach in the UK Biobank, a population-based cohort study (Table S16). In UK Biobank, a one-SD decrease in TG mediated by *LPL* variants reduced risk for both CAD and type 2 diabetes (**Fig. 3**). These genetic results suggest that lowering triglycerides via LPL activation will reduce risks for both CAD and type 2 diabetes.

In summary, combining large-scale human genomic analysis with experimental evidence, we demonstrate: (1) 444 independent coding and non-coding variants at 250 loci as associated with plasma lipids; (2) the use of genome editing to pinpoint causal genes and protein-altering variants, as with the example of *A1CF* p.Gly398Ser; and (3) use of DNA sequence variation to anticipate the efficacy and safety of lipid-modifying medicines, suggesting that PCSK9 inhibitors may raise the risk for type 2 diabetes whereas LPL-activating therapies may decrease the risk for type 2 diabetes and thus be advantageous for patients with metabolic risk factors.

ONLINE METHODS

Study samples and phenotypes

Seventy-three studies contributed association results for exome chip genotypes and plasma lipid levels. The outcomes were fasting lipid values in mg/dL [total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides] from the baseline, or earlier exam with fasting measures. If a study only had non-fasting levels then it contributed only to the total cholesterol and HDL cholesterol analyses. LDL cholesterol and triglyceride analyses were only done on fasting lipid values. The 4S study was published in 1994, which is a clinical trial showing the benefits of statin use. Therefore, for data collected before 1994, no lipid medication adjustment was applied. For data collected after 1994, we adjusted the total cholesterol values for individuals on lipid medication by replacing their total cholesterol values by total cholesterol/0.8. No adjustment was made on HDL cholesterol or triglycerides. LDL cholesterol was calculated using the Friedewald equation for those with TG < 400 mg/dl (LDL = TC – HDL – (TG/5)). If TC was modified as described above for medication use after 1994, then modified TC is used in this formula. If only measured LDL was available in a study, we used LDL/0.7 for those on medication when data were collected after 1994. Triglycerides were natural Log transformed. For each phenotype, residuals were obtained after accounting for age, age^2, sex, principal components (as needed by each study, up to four), and inverse normal transform residuals were created for analysis. For studies ascertained on coronary heart disease case/control status, the two groups were modeled as separate studies.

Genotyping and quality control

All studies assayed the Illumina or Affymetrix Human Exome array v1 or v1.1. Genotypes were determined from Zcall**{** HYPERLINK \l "_ENREF_28" \o "Goldstein, 2012 #189" **}** or joint

calling{ HYPERLINK \l "_ENREF_29" \o "Grove, 2013 #194" }. Individual studies performed the following quality control: call rate, heterozygosity, gender discordance, GWAS discordance (if GWAS data available), fingerprint concordance, if available, and PCA outliers.

Association analyses

Each contributing cohort analyzed the ancestries within their cohorts separately and studies collected on case/control status analyzed cases separately from the controls. We performed both single variant and gene-level association tests. In the association analysis, we obtain residuals after controlling for sex, age, age^2 and up to 4 principal components as covariates. Studies that have (cryptically) related samples analyzed the association using linear mixed models with relatedness estimated from genome-wide SNPs or from pedigrees.

From each study, we collected single variant score statistics and their covariance matrix for variants in sliding windows across the genome. Summary association test statistics were generated using RAREMETALWORKER or RVTESTS. Using summary association statistics collected from each study, we performed meta-analysis of single variant association tests using the Mantel-Haenszel test and constructed burden, SKAT and variable threshold tests using the approach by Liu et al{ HYPERLINK \l "_ENREF_13" \o "Liu, 2014 #683" }. Using covariance matrices between single variant association statistics, we are also able to perform conditional association analysis centrally, which distinguishes genuine signals from "shadows" of known loci. Details of the methods can be found in Liu et al{ HYPERLINK \l "_ENREF_13" \o "Liu, 2014 #683" }.

To ensure the quality of the association analysis, we performed stringent quality control for the data. Centrally, we aligned study reported reference and alternative alleles with alleles reported in the NHLBI Exome Sequencing Project{ HYPERLINK \l "_ENREF_30" \o

"Tennessen, 2012 #736" } and remove mis-labelled variant sites that can be strand ambiguous. For variant sites in each study, we removed variants that had call rate < 0.9 or had Hardy Weinberg p-values $< 1 \times 10^{-7}$. Finally, as additional checks, we visually inspected for each study the scatter plot of variant allele frequency against frequencies from ethnicity-matched populations in the 1000 Genomes Project{ HYPERLINK \l "_ENREF_31" \o "1000 Genomes Project, 2012 #81" }, and made sure that the strand and allele labels were well calibrated between studies.

Single variant associations with $P < 2.1 \times 10^{-7}$ (0.05/242,289 variants analyzed) and gene-based associations with $P < 4.2 \times 10^{-07}$ (0.05/[20,000 genes * 6 tests]) were considered significant. Novel loci were defined as being not within 1 MB of a known lipid GWAS SNP. Additionally, linkage disequilibrium information was used to determine independent SNPs where a locus extended beyond 1 MB.

Sequential forward selection

To identify independently associated variants for each known and newly identified locus, we performed sequential forward selection: We initialized the set of independently associated variants (denoted by Φ), starting with the top association signal in the locus. For each iteration, conditioning on variants in Φ, we performed conditional association analyses for all remaining variants. If the top association signal after the conditional analysis remained significant, we added the top variant to the set Φ, and then repeated the conditional association analysis. If the top variant after the conditional analysis was no longer significant, we stopped and reported variants in the set Φ as the final set of independent variants for that locus. We used the same single variant significance threshold ($P < 2.1 \times 10^{-7}$) to determine statistical significance with the sequential forward selection results (Fig. S2).

Annotation

Sequence variants were annotated according to refSeq version 1.9, using the SEQMINER software{ HYPERLINK \l "_ENREF_32" \o "Zhan, 2015 #738" }. Transcript level annotations were obtained and prioritized. When multiple transcript level annotations were available, they were prioritized according to their functionality and deleteriousness. To implement gene-level association tests, the annotation with the highest priority was used (along with other filtering criteria such as minor allele frequencies) to determine the set of variants that are included.

Heritability and proportion of variance explained estimates

We estimated the proportion of variance explained by the set of independently associated variants. The joint effects of variants in a locus were approximated by $\hat{\vec{\beta}}_{JOINT} = \mathbf{V_{META}^{-1}}\vec{U}_{META}$, where $\vec{U}_{META}$ is the single variant score statistics and $\mathbf{V_{META}^{-1}}$ is the covariance matrix between them. The covariance between single variant genetic effects was approximated by the inverse of the variance-covariance matrix of score statistics, i.e. $\mathbf{V_{META}^{-1}}$. The phenotypic variance explained by the independently associated variants in a locus is given by $\hat{\vec{\beta}}_{joint}^{T}\mathrm{cov(G)}\hat{\vec{\beta}}_{JOINT}$

Refinement of genome-wide association signals

We sought to quantify what proportion of GWAS loci might be due to a protein-altering variant and, therefore, directly identifies a functional gene. We make the reasonably well-supported assumption that a protein-altering variant, if the top signal, explains the signal, or is independent of the original signal, is the most likely causal variant for each region. To identify putative functional coding variants accounting for the effects at known lipid loci, we performed reciprocal conditional analyses to control for the effects of known lipid GWAS or coding variants. Loci where coding variants are the most significant signals were considered as "coding as top". Loci where the initial GWAS variants had conditional P> 0.01 were considered to be explained by the

coding variants. Loci where the coding variants had conditional $P < 2.1 \times 10^{-7}$ were considered to be independent of the initial GWAS signals.

Validation of *A1CF* with CRISPR-Cas9 in human cells

To knock out *A1CF* in Huh7 and HepG2 human hepatoma cells, three CRISPRs (sgRNA sequences are as follows: 5'-GGATGCCCCCAACAAATAAT-3'; 5'-TTGGTTTTATCTGCAGCGCT-3' and 5'-ATGACTCTCATACTCCACGA-3') targeting exon 4 of the *A1CF* gene were constructed by using the lentiviral vector lentiGuide-Puro. Packaged viruses were used to transduce the cells expressing Cas9 for 16 hours. Subsequently, cells were cultured in the presence of 5 μg/ml puromycin for five days before splitting for assays. Cells for APOB secretion assay were cultured for 18 hours in serum-free medium, then the amount of APOB100 in medium was measured using an ELISA kit (MABTECH) according to the manufacturer's instructions.

In a rescue experiment, to avoid cutting of the *A1CF* coding region on the recombinant plasmids by previously designed exon-targeting CRISPRs, four new CRISPRs targeting introns flanking exon 4 were applied to deplete endogenous *A1CF*. The sequences for those sgRNAs are as follows: 5'-GGTTGAAAATGTATGGCTGT-3'; 5'-TGATTGATGAGAATCCTTGT-3'; 5'-TTTTCTTTGCGGAGGCAGGC-3' and 5'-GCAGAGAAGTCTCATCTTTG-3'. The *A1CF* p.Gly398Ser variant was generated by using overlapping PCR and confirmed by Sanger sequencing. Both wild-type and the *A1CF* p.Gly398Ser variant were constructed into lentiviral plasmids, respectively. After transduction, cells were cultured for 48 hours in the presence of 100 ng/ml doxycycline to induce recombinant expression of A1CF or p.Gly398Ser variant before performing different assays.

***A1cf* p.Gly390Ser knock-in mice**

All procedures used for animal studies were approved by Harvard University's Faculty of Arts and Sciences Institutional Animal Care and Use Committee and were consistent with local, state, and federal regulations as applicable. Knock-in mice were generated using a guide RNA designed to target the orthologous site of the *A1CF* p.Gly390Ser variant. In vitro transcribed Cas9 mRNA (100 ng/μL; TriLink BioTechnologies) and guide RNA (50 ng/μL) were co-injected with 100 ng/μL single-strand DNA oligonucleotide (Integrated DNA Technologies): (5'-GTTTGATTCAGTTTAATGCCTTCTTACATTCCTAGAAATTTACATGAATGTCCCTGTAGGGGCTGCGGG GGTGAGAGGTCTGGGCAGCCGTGGCTATTTGGCATACACAGGCCTGGGTCGAGGATACCACGTCAAAGGAGACAAGAGAGAAGACAAACTCTA-3') into the cytoplasm of fertilized oocytes from C57BL/6J mice. Genomic DNA samples from founder mice were screened for knock-in mutations by PCR and confirmed by Sanger sequencing. Positive mice were bred with C57BL/6J mice to generate wild-type and homozygous knock-in mice. Male colony mates at 12 weeks of age were used for lipid measurements. Blood samples were collected from the lateral tail vein following an overnight fast. Plasma triglyceride levels were measured using Infinity Triglycerides Reagent (Thermo Fisher) according to the manufacturers' instructions.

Intersection of lipid association signals with AMD, CAD, and T2D

For 168 variants independently and significantly associated with HDL-C and a MAF > 1%, we looked up the association evidence in 16,144 age-related macular degeneration cases and 17,832 controls with exome chip genotypes**{** HYPERLINK \l "_ENREF_33" \o "Fritsche, 2016 #740" **}**. For 132 independently and significantly associated LDL-C variants and MAF > 1%, we looked up the association evidence in (1). in up to 120,575 individuals with and without coronary

disease and exome chip genotypes (42,335 cases and 78,240 controls)**{** HYPERLINK \l "_ENREF_21" \o "Myocardial Infarction, 2016 #21" **}**, and (2). in up to 69,870 individuals with and without type 2 diabetes. Only 113 of the 132 LDL variants were available in the type 2 diabetes results. We used a Bonferroni correction for 132 variants to determine significance of the results (alpha = 4.0×10^{-4}).

T2D PCSK9 association analysis.

For evaluating the effect of PCSK9 R46L variant on risk of T2D, we considered a total of 42,011 T2D cases and 180,834 controls from 30 studies from populations of European ancestry (Table S17). The variant was directly genotyped in all studies using the Metabochip or the Exome array. Sample and variant quality control was performed within each study as described previously**{** HYPERLINK \l "_ENREF_34" \o "Morris, 2012 #756" **}**. Within each study, the variant was tested for T2D association under an additive model after adjustment for study-specific covariates, including principal components to adjust for population structure. Association summary statistics for the variant for each study was corrected for residual population structure using the genomic control inflation factor as described previously**{** HYPERLINK \l "_ENREF_34" \o "Morris, 2012 #756" **}**. We then combined association summary statistics for the variant across studies via fixed-effects inverse-variance weighted meta-analysis.

LPL Pathway variants

Exome chip results for LPL pathway variants in six genes (*LPL, ANGPTL4, APOA5, APOC3, ANGPTL3, and ANGPTL8*) were obtained from: (1) in up to 120,575 individuals with and without coronary disease and exome chip genotypes (42,335 cases and 78,240 controls)**{** HYPERLINK \l "_ENREF_21" \o "Myocardial Infarction, 2016 #21" **}**; and (2) in up to 69,870 individuals with and without type 2 diabetes. Scores were created based on summary statistics**{**

HYPERLINK \l "_ENREF_38" \o "International Consortium for Blood Pressure Genome-Wide Association, 2011 #744" **}** using the gtx R package with the grs.summary function (https://cran.r-project.org/web/packages/gtx/) and the independent variants within each of the *LPL* pathway genes.

{ ADDIN EN.REFLIST }

Fig. 1: *A1CF* p.Gly398Ser is associated with increased APOB100 secretion. A, Western blot showing the depletion of endogenous A1CF levels via CRISPR/Cas9 system in both Huh7 and HepG2 cells. **B and C**, Lack of A1CF leads to reduced APOB100 secretion in Huh7 (B) and HepG2 (C) human hepatoma cells. **D**, Recombinantly overexpressed A1CF p. Gly398Ser variant led to significantly increased APOB100 secretion compared to A1CF or GFP control in both Huh7 wild-type and A1CF knockout cells (labeled as A1CF KO), respectively. The error bars show SD from experiments with biological replicates, N=6 for B, C and D. Statistically significant differences are marked (*p<0.05, **p<0.01).

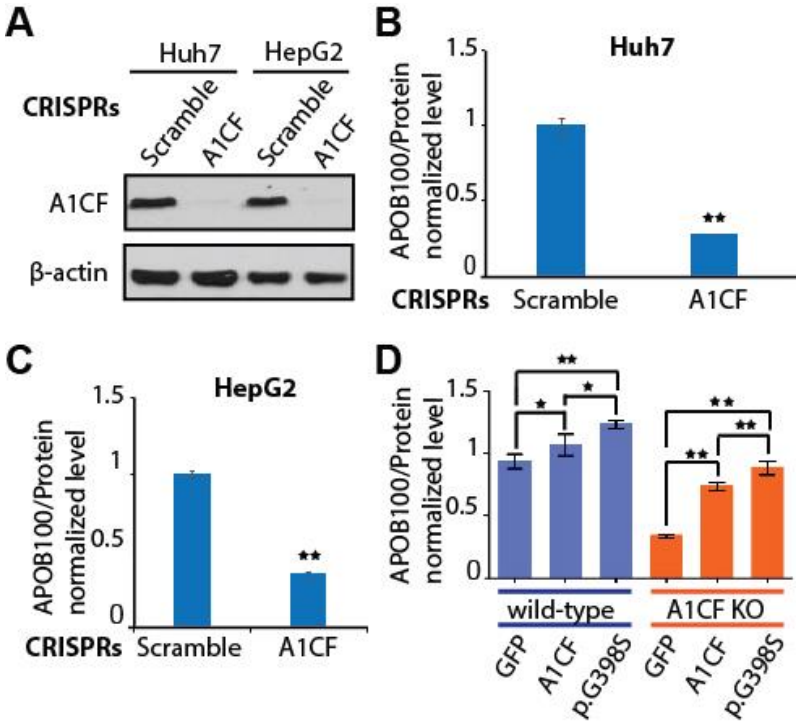


Fig. 2: Association of PCSK9 R46L with risk for type 2 diabetes. In each study, the relationship of PCSK9 R46L with risk of type 2 diabetes was determined. P-values for association tests and confidence intervals were determined using exact methods. A meta-analysis across studies was performed with the use of the Cochran–Mantel–Haenszel statistics for stratified 2-by-2 tables. This method combines score statistics and is particularly useful when some observed odds ratios are zero.

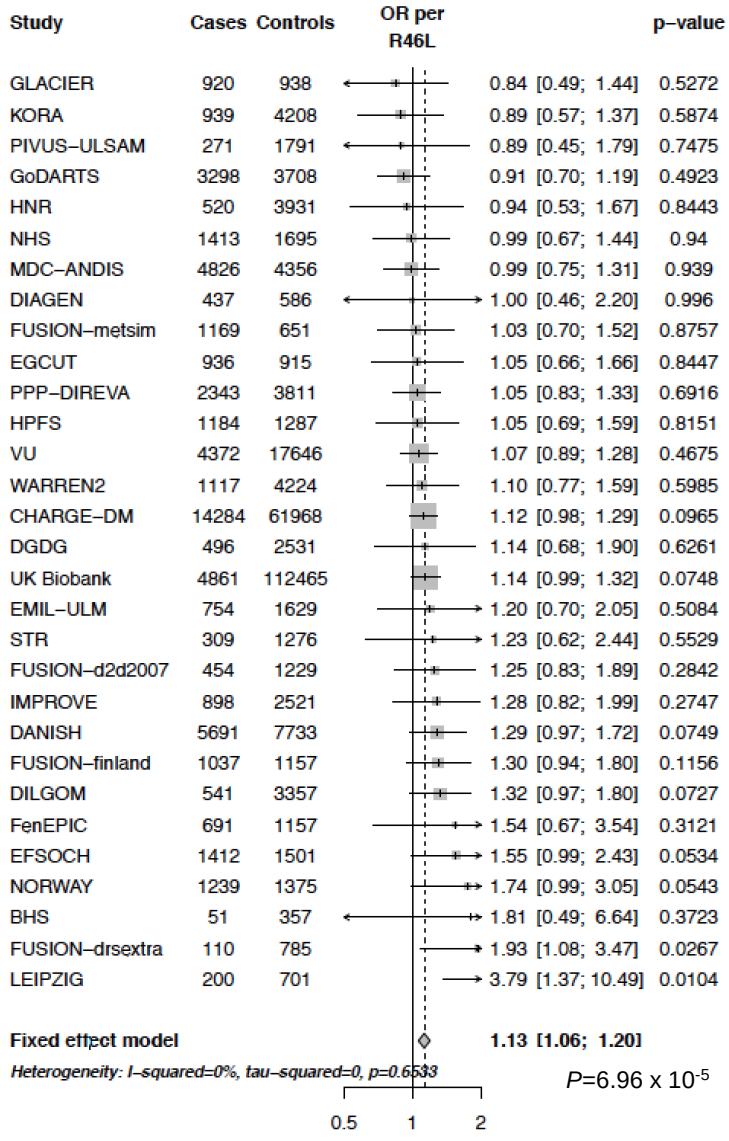
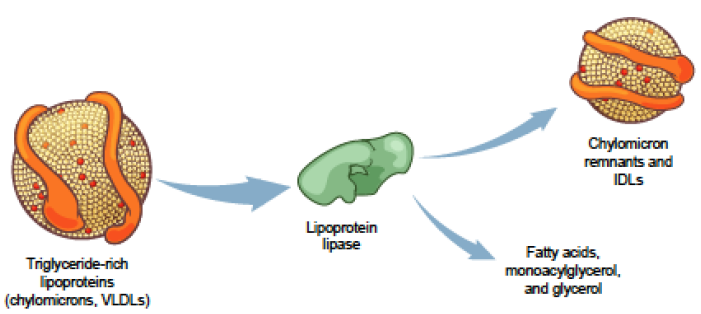
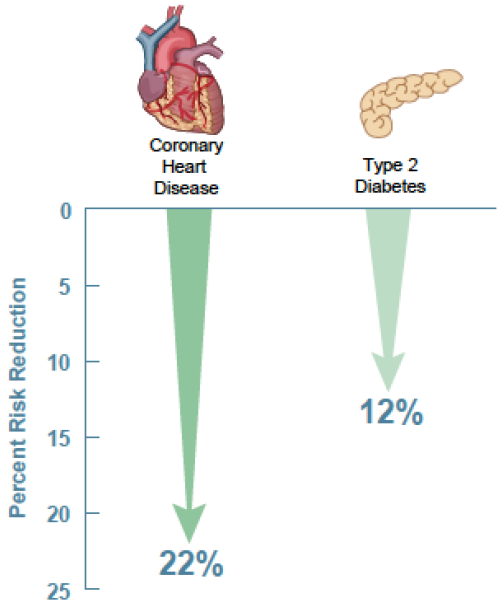


Fig. 3: Association of a one standard deviation genetically-lowered triglyceride mediated by *LPL* variants with a range of phenotypes. Estimates were derived in UK Biobank using logistic regression, adjusting for age, sex, ten principal components of ancestry and an indicator variable for array type. Definitions for all outcomes are provided in Table S16.





	Cases	Controls	OR per SD Lower TG	P Value
Cardiovascular				
Coronary Heart Disease	4461	107877	0.78 [0.69; 0.88]	0.0001
Stroke	2066	110272	1.06 [0.90; 1.25]	0.51
Heart Failure	599	111739	0.83 [0.60; 1.13]	0.24
Atrial Fibrillation	2208	110130	0.93 [0.79; 1.09]	0.35
Aortic Stenosis	193	112145	0.63 [0.36; 1.13]	0.12
Peripheral Vascular disease	692	111646	0.85 [0.64; 1.14]	0.28
Venous Thromboembolism	3306	109032	1.00 [0.87; 1.14]	0.97
Gastrointestinal disease				
Inflammatory Bowel Disease	1021	111317	1.17 [0.93; 1.48]	0.17
Gastric Reflux	4881	107457	1.03 [0.92; 1.14]	0.64
Gallstones	1831	110507	1.13 [0.95; 1.34]	0.17
Irritable Bowel Syndrome	2679	109659	0.93 [0.80; 1.08]	0.36
Endocrine				
Type 2 Diabetes	5741	112338	0.88 [0.79; 0.97]	0.014
Gestational Diabetes	56	112282	0.73 [0.26; 2.08]	0.56
Hyperthyroidism	868	111470	1.13 [0.88; 1.45]	0.33
Hypothyroidism	5433	106905	1.05 [0.95; 1.17]	0.35
Gout	1612	110726	1.00 [0.83; 1.21]	0.98
Renal/urological				
Enlarged Prostate	1573	110765	1.08 [0.89; 1.30]	0.45
Uterine Fibroids	1634	110704	1.00 [0.83; 1.20]	0.99
Neurological/psychiatric				
Migraine	3161	109177	1.02 [0.89; 1.17]	0.74
Depression	6667	105671	1.06 [0.97; 1.17]	0.20
Anxiety	1545	110793	1.02 [0.84; 1.23]	0.84
Musculooskeletal				
Backpain	584	111754	1.03 [0.76; 1.40]	0.85
Jointpain	377	111961	0.99 [0.68; 1.46]	0.97
Osteoporosis	1740	110598	1.02 [0.85; 1.22]	0.85
Osteoarthritis	9693	102645	0.96 [0.89; 1.05]	0.38
Sciatica	1035	111303	1.00 [0.79; 1.27]	0.98
Prolapsed Disc	1856	110482	1.04 [0.87; 1.24]	0.65
Respiratory				
Asthma	13941	96397	0.99 [0.93; 1.06]	0.84
COPD/Emphysema	2363	109975	0.93 [0.80; 1.09]	0.40
Pneumonia	1581	110757	1.05 [0.87; 1.26]	0.63
Hayfever	6263	106075	1.06 [0.96; 1.17]	0.24
Cancer				
Lung Cancer	115	112223	0.92 [0.45; 1.86]	0.81
Breast Cancer	2383	109955	0.90 [0.77; 1.06]	0.20
Colorectal Cancer	616	111722	1.16 [0.86; 1.56]	0.32
Skin Cancer	2482	109856	0.96 [0.82; 1.12]	0.59
Prostate Cancer	840	111498	0.99 [0.76; 1.28]	0.92
Cervical Cancer	872	111466	1.09 [0.85; 1.40]	0.49
Other Cancer	2409	109929	0.88 [0.75; 1.03]	0.10
Any Cancer	9530	102808	0.94 [0.87; 1.02]	0.17

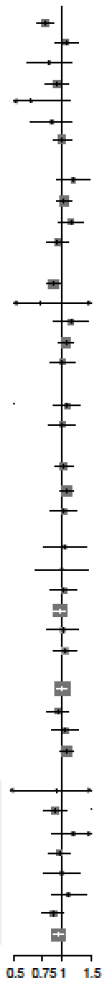


Table 1: Protein-altering variants at novel loci associated with lipid levels.

Chromosome :position (hg19)	rs ID	Alleles (reference/ alternative)	Gene	Protein change	N	Frequency alternative allele	Trait	P value	Beta±SE
Total Cholesterol									
2:101627925	rs1062062	C/T	*TBC1D8*	p.Gly954Arg	292898	0.12	TC	1×10^{-7}	-0.021±0.0040
4:69343287	rs976002	A/G	*TMPRSS11E*	p.Tyr303Cys	293961	0.23	TC LDL-C	5×10^{-20} 3×10^{-12}	0.029±0.0031, 0.023±0.0033
4:155489608	rs6054	C/T	*FGB*	p.Pro206Leu	307997	0.0038	TC TG	5×10^{-12} 3×10^{-11}	0.14±0.021, 0.14±0.021
9:5073770	rs77375493	G/T	*JAK2*	p.Val617Phe	188412	0.0011	TC LDL-C	1×10^{-11} 2×10^{-9}	-0.32±0.047, -0.30±0.049
9:117166246	rs2274159	A/G	*DFNB31*	p.Val400Ala	319677	0.48	TC	2×10^{-7}	0.013±0.0026
17:8216468	rs871841	T/C	*ARHGEF15*	p.Leu277Pro	298725	0.52	TC	2×10^{-8}	0.015±0.0026
19:18304700	rs874628	A/G	*MPV17L2*	p.Met72Val	319677	0.26	TC	2×10^{-7}	0.015±0.0029
LDL Cholesterol									
1:155106227	rs4745	A/T	*EFNA1*	p.Asp137Val	291361	0.49	LDL-C	5×10^{-8}	-0.015±0.0027
4:187120211	rs13146272	C/A	*CYP4V2*	p.Gln259Lys	295826	0.62	LDL-C	1×10^{-7}	-0.015±0.0027
5:176520243	rs351855	G/A	*FGFR4*	p.Gly388Arg	233058	0.29	LDL-C	4×10^{-8}	-0.018±0.0033
9:139368953	rs3812594	G/A	*SEC16A*	p.Arg1039Cys	293723	0.24	LDL-C	2×10^{-8}	-0.018±0.0031
10:118397971	rs10885997	A/G	*PNLIPRP2*	p.Gln387Arg	258146	0.41	LDL-C	9×10^{-8}	0.015±0.0029
10:124610027	rs1891110	G/A	*FAM24B*	p.Pro2Leu	295826	0.55	LDL-C TC	8×10^{-15} 2×10^{-13}	0.021±0.0026, 0.019±0.0025
12:72179446	rs61754230	C/T	*RAB21*	p.Ser224Phe	292762	0.015	LDL-C	1×10^{-7}	0.057±0.011
14:94844947	rs28929474	C/T	*SERPINA1*	p.Glu366Lys	290263	0.015	LDL-C TC	4×10^{-14} 6×10^{-14}	0.081±0.011, 0.078±0.010
17:26694861	rs704	G/A	*VTN*	p.Thr400Met	295826	0.49	LDL-C TC	6×10^{-16} 1×10^{-8}	0.021±0.0026, 0.015±0.0025
19:42584958	rs201596848	C/T	*ZNF574*	p.Arg734Cys	273744	0.0014	LDL-C	5×10^{-12}	-0.255±0.037
Triglycerides									
2:202122995	rs3769823	A/G	*CASP8*	p.Lys14Arg	295956	0.69	TG	1×10^{-9}	0.017±0.0028
5:131008194	rs26008	T/C	*FNIP1*	p.Gln620Arg	305699	0.92	TG	5×10^{-9}	-0.028±0.0048
10:52573772	rs41274050	C/T	*A1CF*	p.Gly398Ser	299984	0.0072	TG TC	4×10^{-11} 1×10^{-7}	0.10±0.015, 0.08±0.015
13:45970147	rs138358301	A/G	*SLC25A30*	p.Phe280Leu	301087	0.0035	TG	3×10^{-11}	0.15±0.022

15:40751555	rs3803357	C/A	*BAHD1*	p.Gln298Lys	305699	0.55	TG	1×10^{-10}	-0.017±0.0026
17:17409560	rs7946	C/T	*PEMT*	p.Val212Met	304420	0.67	TG	1×10^{-8}	-0.016±0.0029
20:56140439	rs41302559	G/A	*PCK1*	p.Arg483Gln	299984	0.0021	TG	9×10^{-8}	-0.154±0.029
22:17625915	rs35665085	G/A	*CECR5*	p.Thr149Met	302582	0.050	TG	5×10^{-8}	0.032±0.0059
HDL Cholesterol									
2:272203	rs11553746	C/T	*ACP1*	p.Thr95Ile	313148	0.33	HDL-C	5×10^{-8}	0.015±0.0027
2:54482553	rs17189743	G/A	*TSPYL6*	p.Arg246Cys	314415	0.029	HDL-C	2×10^{-7}	0.040±0.0076
2:179309165	rs75862065	G/A	*PRKRA*	p.Pro116Leu	105490	0.29	HDL-C	2×10^{-7}	0.026±0.0050
3:48229366	rs146179438	C/A	*CDC25A*	p.Gln25His	288306	0.020	HDL-C	3×10^{-11}	-0.063±0.0095
5:176637576	rs28932178	T/C	*NSD1*	p.Ser457Pro	310567	0.17	HDL-C	8×10^{-9}	0.020±0.0035
11:64031241	rs35169799	C/T	*PLCB3*	p.Ser778Leu	314415	0.060	HDL-C TG	4×10^{-13}, 3×10^{-12}	-0.039±0.0054, 0.038±0.0055
11:68703959	rs622082	A/G	*IGHMBP2*	p.Thr671Ala	316391	0.31	HDL-C	6×10^{-10}	-0.017±0.0028
16:4755108	rs78074706	G/A	*ANKS3*	p.Arg286Trp	315298	0.022	HDL-C	1×10^{-9}	-0.053±0.0087
16:69385641	rs76116020	A/G	*TMED6*	p.Phe6Leu	310822	0.033	HDL-C	7×10^{-9}	-0.041±0.0071
17:40257163	rs2074158	T/C	*DHX58*	p.Gln425Arg	244331	0.19	HDL-C	1×10^{-7}	-0.020±0.0038

Variant information and genetic effects of alternative alleles are reported. Genetic variants were annotated based upon RefSeq 1.9. Beta is displayed as % of 1 standard deviation change in plasma lipid level. Alleles were modeled to the forward strand. Variants are categorized according to the lipid trait with strongest strength of association.